K062756

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510(K) SUMMARY OF SAFETY AND EFFECTIVENESS

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92(c).

Submitted by:
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Date Summary Prepared: 25 August 2006
Date Summary Revised: 11 January 2007

Trade Name: PATHIAM Image Analysis Software for Her2/neu

Classification Name: Unknown

Device Description:
PATHIAM software is a standalone software application that will work on a system with the following features required but not provided:
Computer

- Processor: 2.4 GHz, Pentium IV equivalent
- Memory: 512 MB RAM
- Operating System: Windows 2000 or later
- Hard Drive: minimum 100MB for software installation, 20GB for image storage
- LAN connectivity, minimum 100 MBPS (recommended), support for USB interface, support for HTTP, TCP/IP protocols (using the Operating system)
- High Speed Graphic Accelerator Card (1024 X 768)
- 17" High resolution display monitor
- 24 bit color depth
- Font Setting: Small font (DPI setting: 96 DPI)

Digitizing Equipment: Camera

- Resolution: at least 2048 x 1536 pixels
- Frame rate: 20 fps@1200 x 768 resolution (6 fps @ 2048 x 1536 resolution)
- Sampling Frequency of 6.26 square/μm

- Compression format: JPEG 2000, BMP, TIFF. JPEG
- Color: 24-bit (R, G, B)
- Connection to computer

Digitizing Equipment: Digital Side Scanner

- Input Format: 25X75mm microscope slides
- Resolution: 54,000 pixel/inch with 20X objective
- Method: Line-scanning
- File Format: TIFF/JPEG2000; compliant with TIFF 6.0 standard.
- Color: 24-bit (R,G, B)
- Connectivity: 100/1000 MBPS Ethernet
- Compression format: JPEG 2000, BMP, TIFF. JPEG

The software allows both archiving of the digital image, and semi quantitative analysis of extent and intensity of stained tissue, providing the pathologist with an aid to interpretation of level of expression of Her2/neu in breast cancer tissue. The pathologist is presented with a digital image of the tissue section and a suggested staining score (0 to 3). The pathologist then makes an assessment of the digital image and reports his/her score.

Indications for Use:

BioImagene PATHIAM is intended for use as an accessory to the Dako HercepTest® to aid a pathologist in semi-quantitative measurement of HER2/neu (c-erbB-2) in Formalin-fixed, paraffin-embedded breast cancer tissue.
When used with the Dako HercepTest it is indicated as an aid in the assessment of breast cancer patients for whom Herceptin® (Trastuzumab) treatment is being considered.
NOTE: The actual correlation of the Dako HercepTest to Herceptin clinical outcome has not been established.

Predicate Devices:

Software Her2/neu application of ChromaVision Medical Systems, Inc. Automated Cellular Imaging System (ACIS) for Her2/neu, K032113

Performance

a. Between laboratory reproducibility: PATHIAM software was tested by three different pathologists, who analyzed images of the same set of 176 stained breast cancer tissue specimens using three different imaging systems in three different laboratories located at three different sites in the US. One laboratory used a microscope with a camera, and two used different models of digital whole slide scanners. The score distribution for these samples, as determined initially, was 1/6 of samples score 0, 1/3 of samples score 1, 1/3 of samples score 2, and 1/6 of samples score 3.

   Overall agreement for the PATHIAM values between labs ranged from 94% to 95% (Table 1). For pathologist assisted by PATHIAM, overall agreement

between labs was 81% to 96% (Table 2). Overall agreement between laboratories for a manual (microscope assessment only) value ranged from 76% to 97% (Table 3).

Table 1. Between-Lab Agreement for Raw PATHIAM- Scores, HercepTest®-stained Breast Tissue

Lab # vs. Lab#	% Overall Agreement	95% Confidence Interval (Exact)
1 v 2	95	91-98
1 v 3	94	89-96
2 v 3	94	89-97

Table 2. Between-Lab Agreement for Pathologist Assisted by PATHIAM Scores, HercepTest-stained Breast Tissue

Lab # vs. Lab#	% Overall Agreement	95% Confidence Interval (Exact)
1 v 2	96	92-98
1 v 3	81	75-87
2 v 3	81	74-89

Table 3. Between-Lab Agreement for Manual Scores, HercepTest-stained Breast Tissue

Lab # vs. Lab #	% Overall Agreement	95% Confidence Interval (Exact)
1 v 2	97	93-99
1 v 3	76	69-82
2 v 3	78	71-84

b. Comparison with manual (microscope assessment only) Her2-neu scores were obtained for those same breast cancer tissues from a review of PATHIAM values by the same three trained pathologists, who viewed both the digital images and the score provided by the software, and then selected an appropriate Her2-neu tissue score (0 to 3). One week later, the same pathologist read the same slides manually, using an optical microscope. The table shows the comparison.

Table 4. Percent Agreement Between PATHIAM-Assisted and Manual Scores, HercepTest®-stained Breast Tissue

Lab #	% Overall Agreement	95% Confidence Interval (Exact)
1	81	75-87
2	84	78-89
3	82	76-88

Table 5. Percent Agreement between PATHIAM raw scores and Manual Scores, HercepTest-stained breast Tissue

Lab #	% Overall Agreement	95% Confidence Interval (Exact)
1	81	74-86
2	83	77-88
3	78	71-84

c. Conclusion: It can be seen that the agreement of the manual scores compared to the PATHIAM raw scores (Table 5) is more consistent than the inter-pathologist comparison of manual scores (Table 3). Consistency is improved when the PATHIAM score assists the pathologist in their interpretation (Table 2). The comparison of PATHIAM raw scores across the three different setups in three different laboratories is very good (Table 1). Differences may be due to the selection by the pathologists of different fields of view for the analyses.

d. Specificity, sensitivity and interferences are described in the HercepTest package insert.

e. Substantial equivalence: Table 6 shows a comparison of attributes between PATHIAM and the predicate

Table 6. Comparison to Predicate Devices to Support Substantial Equivalence Determination

Attribute	ACIS Her2/neu software component	PATHIAM
Intended use	The imaging software is intended to detect and classify cells of clinical interest by analyzing digital images of microscope slides based on object identification of cellular	Same

	objects of particular intensity, shape, size and color. The software can be used with a computer and image digitizer with features specified in the labeling	
Indications for use	As an accessory to an assay which is indicated as an aid in the assessment of breast cancer patients for whom Herceptin® treatment is considered	As an accessory to the Dako HercepTest® to aid a pathologist in semi-quantitative measurement of HER2/neu (c-erbB-2) in Formalin-fixed, paraffin-embedded breast cancer tissue. When used with the Dako HercepTest it is indicated as an aid in the assessment of breast cancer patients for whom Herceptin® (Trastuzumab) treatment is being considered.
Specimen Type	Formalin-fixed, paraffin-embedded specimens stained by immunohistochemistry reagent for Her2/neu	Same
Image Analysis System	Histologic observation by a pathologist through a controlled microscope/digital camera combination	Histologic observation by a pathologist through a specified microscope/digital camera combination or slide scanner
Method of Cell Detection	Colorimetric pattern recognition by microscopic examination of prepared cells by size, shape, hue and intensity as observed by a computer-assisted microscope and by visual observation by a health care professional	Object identification of a digitized filed of view of a pathology slide, using size, shape, color and intensity as observed by a software and by visual observation of the digitized image by a health care professional.
Hardware components	Computer, microscope, color monitor, keyboard, automatic storage of acquired images	Required but not provided: computer, either microscope with digitizing camera or slide scanner,

		keyboard, mouse, hi-resolution color monitor, and hard drive for storage.
Assay used	DAKO HercepTest	Same

f. Standards Employed: None under Section 514

g. FDA Guidance Guidance for the Content of Premarket Submissions for Software contained in Medical Devices, May 11, 2005

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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FEB 2 0 2007

Re: k062756
Trade/Device Name: PATHIAM™ Imaging Software for Her2/neu
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry Reagents and Kits
Regulatory Class: Class II
Product Code: NOT
Dated: February 12, 2007
Received: February 13, 2007

Dear Ms. Longwell:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The

FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Robert L. Becker, Jr., M.D., Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K062756

Device Name: PATHIAM™ Imaging software for Her2/neu

Indications For Use: BioImagene PATHIAM is intended for use as an accessory to the Dako HercepTest® to aid a pathologist in semi-quantitative measurement of HER2/neu (c-erbB-2) in Formalin-fixed, paraffin-embedded breast cancer tissue.
When used with the Dako HercepTest it is indicated as an aid in the assessment of breast cancer patients for whom Herceptin® (Trastuzumab) treatment is being considered.
NOTE: The actual correlation of the Dako HercepTest to Herceptin clinical outcome has not been established.

Intended Use: The imaging software is intended to detect and classify cells of clinical interest by analyzing digitized images of microscope slides based on recognition of cellular objects of particular color, size and shape. The software can be used with a computer and image digitizer with features specified in the labeling.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Maria M Chan

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K062756